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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,183	11/14/2000	Rino Rappuoli	PP00362.102	3087

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Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER

DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 08/01/2003.

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/674,183

Applicant(s)

Rappuoli et al

Examiner

S. Devi, Ph.D.

Art Unit

1645

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 6, 2003
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 ~~is/are~~ pending in the application.
- 4a) Of the above, claim(s) 9, 18, 20, 22, and 24-32 ~~is/are~~ withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10-17, 19, 21, and 23 ~~is/are~~ rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9 & 10. 6) ☐ Other:

DETAILED ACTION

Preliminary Amendment

- 1) Acknowledgment is made of Applicants' preliminary amendment filed 07/23/02 (paper no. 7). With this, Applicants have amended the specification.

Election

- 2) Acknowledgment is made of Applicants' election, with traverse, of invention I, claims 1-17, 19, 21 and 23, filed 05/06/03 (paper no. 12) in response to the lack of unity mailed 04/09/03 (paper no. 11). Applicants' traversal is on the ground s that the present claims patentably distinguish over the teachings of Paradiso *et al.* and therefore define a special technical feature. Applicants point to Annex B, Part 2 of the PCT Administrative Instructions and state that unity exists between a protein and the DNA encoding the protein, and a substance, a method of manufacturing the substance and a method of using the substance. Applicants state that the special technical feature common to all the claims in the subject application is a five T cell epitope-containing carrier protein and therefore, at least the claims of Groups I, II, III and IV should be examined together.

Applicants' arguments have been carefully considered, but are non-persuasive. As is evident from the art rejection(s) made below, a carrier protein containing at least five T cell epitopes was taught or suggested in the prior art. Clearly, the special technical feature does not define over the prior art and therefore is not a unifying feature. The lack of unity held in the instant application is proper and is maintained.

The Applicants' statement that the special technical feature common to all the claims in the subject application is a five T cell epitope-containing carrier protein has been noted. Since the carrier protein claimed in the independent claim 9 is not required to contain at least five CD4+ T cell epitopes, it is viewed as a second product which does not share the special technical feature or a common structure with the product of, for example, claim 1. Claim 9 is now removed from invention I and is therefore not examined.

Status of Claims

- 3) Claims 1-32 are pending.

Claim 18, 20, 22 and 24-32 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. § 821.03. Claim 9 has been removed

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from invention I since it does not share the special technical feature.

Claims 1-8, 10-17, 19, 21 and 23 are under examination. An Action on the Merits for these claims is issued.

Sequence Listing

4) Acknowledgment is made of Applicants' submission of the raw sequence listing and CRF which has been entered.

Priority

5) The instant application is a national stage 371 application of PCT/IB99/00844, filed 04/27/1999 and claims foreign priority to application 988932.9 filed 04/27/1998 in Great Britain. It is noted that Applicants have submitted a certified copy of the priority document.

Information Disclosure Statements

6) Acknowledgment is made of Applicants' Information Disclosure Statements filed 09/16/02 (paper no. 9) and 11/08/02 (paper no. 10). The documents referred to therein, except for a duplicate submission, have been considered. A signed copy is attached to this Office Action (paper no. 13).

Drawings

7) The drawings are objected to under 37 C.F.R. 1.84 because of the reasons set forth by the Draftsperson in the attached Form PTO 948 (paper no.13). Correction is required. Applicant is asked to note the changes effected 03 May 2001, particularly the changes to the 'Timing of Corrections':

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 C.F.R. 1.85; 1097 O.G. 36

New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the "Notice of Allowability" (PTOL-37 or PTO-37). If delayed, the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability" to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 C.F.R. 1.136(a) for filing the corrected drawings (but

not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, Applicant must arrange to have an acceptable correction re-submitted within the original three month period to avoid the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Abstract

- 8) This application currently does not contain an abstract of the disclosure as required by 37 C.F.R 1.72(b). However, as this application is filed under 371 with a priority claim to PCT/IB99/00844, a copy the published abstract from PCT/IB99/00844 is placed in the instant application as page number 62. If Applicants desired changes to the abstract, such changes should be directed to the abstract of the PCT/IB99/00844.

Specification - Informalities

- 9) The specification is objected to for the following reasons:
- (a) The use of the trademarks in the instant specification has been noted in this application. For example, see line 4 on page 41: "Sepharose"; page 44, line 1 and page 43, lines 26

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and 29: "Tween-20"; and page 40, line 2; lines 19 and 22 on page 29: 'Tween 80'; line 17 on page 29: 'Span 85'; and line 23 on page 39 and line 2 on page 40: 'Q-Sepharose'. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(b) Some Figures are incorrectly numbered. The different panels in Figures 1, 2 and 7 should be individually renumbered. For example, Figure 2 includes three parts/panels and should be labeled as Figures 2A, 2B and 2C. Figures 7 and 8 include two parts/panels and should be labeled as Figures 7A and 7B; and Figures 8A and 8B respectively. All references to these Figures in the specification should be amended to reflect these changes in numbering. The description for 'Figure 10' in lines 4, 5, 10 and 14 on page 33 should be replaced with --Figures 10A, 10B and 10C--; --Figure 10A--; --Figure 10B--; and --Figure 10C-- respectively.

(c) The meaning of 'centrifugation' at line 21 on page 38 is not understood.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

10) Claims 1-17, 19, 21 and 23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 1, 2 and 13 are vague and indefinite in the recitation "derived", because it is unclear what the process of "deriving" encompasses: extraction, separation, recombinant expression, purification or modification?

(b) Claims 2-17 lack proper antecedent basis in the recitation: 'A carrier protein according to claim ...'. To be consistent with the claim language used in claims 19 and 23, it is suggested that Applicants replace the recitation in claims 2-17 with --The carrier protein according to claim ---.

(c) For proper antecedence, in claims 2-8, it is suggested that Applicants replace the recitation 'the CD4+ epitopes' with --the CD4+ T cell epitopes'.

(d) The independent claims 4-7 vague and indefinite in the abbreviated recitations 'MT' or 'HA', because it is unclear what does this stand for. It is suggested that each abbreviation be

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recited as a full terminology at first occurrence in an independent claim, with its abbreviated recitation retained in parentheses.

(e) Claim 11 is vague in lacking a preceding article in between the recitation 'to polysaccharide'. It is suggested that Applicants replace the recitation with --to a polysaccharide--.

(f) Claims 14 and 15 are vague and indefinite and/or lack antecedence in the recitation: conjugated 'to protein', because it is unclear whether this a protein other than the carrier protein. If this is meant to be the carrier protein, then it is suggested that Applicants replace the recitation with -to said carrier protein--.

(g) Claim 16 is vague and indefinite in the recitation: 'protein units' or 'polysaccharide unit', because it is unclear what is contained in a 'unit', or whether it represents whole protein or polysaccharide or a part of the same.

(h) Claim 21 is vague and indefinite and/or lacks antecedence in the recitation: 'a carrier protein according to claim ...'. It is suggested that Applicants replace the phrase with --the carrier protein according to claim ...--.

(i) Claims 2-17, 19, 21 and 23, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

11) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12) Claims 1-4, 8, 10-12, 14, 16, 17, 19, 21 and 23 are rejected under 35 U.S.C § 102(b) as being anticipated by Peeters *et al.* (*Infect. Immun.* 60: 1826-1833, 1992) as evidenced by Falugi *et al.* (*Eur. J. Immunol.* 31: 3816-3824, 2001).

Peeters *et al.* taught the purified carrier protein, TT, in an unconjugated and a conjugated form being conjugated to *Haemophilus influenzae* type B polysaccharide or oligosaccharide. The conjugate elicited protective serum antibodies in human infants. The conjugate had about 7 protein

units per polysaccharide (see abstract; Table 1; and page 1826; 'Materials and Methods' and 'Results'). That the prior art TT contains at least five CD4+ T cell epitopes and is made up of oligomeric peptides is inherent from the teachings of Peeters *et al.* in light of what is well known in the art. For instance, Falugi *et al.* showed that TT contains at least five CD4+ T cell epitopes in TT, i.e., P23TT, P32TT, P21TT, P30TT and P2TT (see Table 1).

The teachings of Peeters *et al.* anticipate the instant claims. Falugi *et al.* is **not** used as a secondary reference in combination with Peeters *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Peeters *et al.* with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

13) Claims 1-4, 8, 10, 11, 13-17, 19 and 21 are rejected under 35 U.S.C § 102(b) as being anticipated by Jennings *et al.* (*In: Seminars in Infectious Disease*. (Ed) Weinstein *et al.* Volume IV, Chapter 34, 247-253, 1982) as evidenced by Falugi *et al.* (*Eur. J. Immunol.* 31: 3816-3824, 2001).

Jennings *et al.* taught the protein carrier, TT, and a conjugate vaccine wherein TT is covalently linked or conjugated to a polysaccharide of *N. meningitidis* by reductive amination (see abstract; and pages 248-250). One conjugate contained 2 protein units per polysaccharide (see Table 1). That the prior art TT contains at least five CD4+ T cell epitopes and is made up of oligomeric peptides is inherent from the teachings of Jennings *et al.* in light of what is well known in the art. For instance, Falugi *et al.* showed that TT contains at least five CD4+ T cell epitopes in TT, i.e., P23TT, P32TT, P21TT, P30TT and P2TT (see Table 1).

The teachings of Jennings *et al.* anticipate the instant claims. Falugi *et al.* is **not** used as a secondary reference in combination with Jennings *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Jennings *et al.* with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

14) Claims 1 and 7 are rejected under 35 U.S.C § 102(b) as being anticipated by Nussenzweig *et al.* (WO 86/05790) as evidenced by Falugi *et al.* (*Eur. J. Immunol.* 31: 3816-3824, 2001).

Nussenzweig *et al.* taught the protein carrier, TT, and a conjugate wherein TT is conjugated to a *Plasmodium falciparum* circumsporozoite antigen (i.e., PfCs). See abstract; and claims. That

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the prior art TT contains at least five CD4+ T cell epitopes and is made up of oligomeric peptides is inherent from the teachings of Nussenzweig *et al.* in light of what is well known in the art. For instance, Falugi *et al.* showed that TT contains at least five CD4+ T cell epitopes in TT, i.e., P23TT, P32TT, P21TT, P30TT and P2TT (see Table 1).

The teachings of Nussenzweig *et al.* anticipate the instant claims. Falugi *et al.* is **not** used as a secondary reference in combination with Nussenzweig *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Nussenzweig *et al.* with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Remarks

- 15) Claims 1-8, 10-17, 19, 21 and 23 stand rejected.
- 16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center receives facsimile transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.
- 17) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July, 2003


S. DEVI, PH.D.
PRIMARY EXAMINER